

**REMARKS**

Claims 11-19 and 21-31 are pending in this application. Non-elected claims 12, 14-16, 18, 19, 21, 22, 24, 25, 27, 28, 30 and 31 are withdrawn from consideration by the Examiner.

**I. Rejection Under 35 U.S.C. §103**

The Office Action rejects claims 11, 13, 17, 23, 26 and 29 under 35 U.S.C. §103(a) as having been obvious over U.S. Patent No. 6,686,505 to Watanabe et al. ("Watanabe") in view of JP 11-189600 to Ikariya et al. ("Ikariya"). Applicants respectfully traverse the rejection.

Claim 11 is directed to a process for producing an optically active alcohol comprising placing a metal complex and a ketone compound in a polar solvent and without the presence of a base and stirring the mixture under pressurized hydrogen (hydrogen gas) to hydrogenate the ketone compound. It is well known in the art that it is difficult to hydrogenate a ketone compound, such as 4-chromanone and alpha-chloroacetophenone, into an optically active alcohol. See Ohkuma I, page 8724, left column, last paragraph, and Reference (13); and Cross et al., Scheme 6 (attached). However, optically-active alcohol can be attained with high yield and high stereo selectivity by the claim process. The applied references do not disclose the claim process for at least the following reasons.

Watanabe discloses a method for producing an optically active amino alcohol by hydrogenating a ketone compound using a hydrogen donor as a hydrogen source. See col. 4, line 47 - col. 5, line 25; col. 5, lines 42-52; col. 20, lines 10-22; col. 22, lines 16-19; and claims 1 and 2. Watanabe further discloses methanol, formic acid, and a salt thereof, as a hydrogen donor. See col. 20, lines 56-62. Watanabe, however, is silent with respect to the use of hydrogen gas as a hydrogen source. Thus, Watanabe does not disclose a process for producing an optically active alcohol by using pressurized hydrogen to hydrogenate a ketone compound.

The Office Action, at page 2, asserts Watanabe discloses a process for producing an optically active alcohol in the absence of a base. The Office Action further asserts, at page 3, that a base may be required to form the ruthenium chloride catalyst that is used to carry out the reaction process of Watanabe, but a base is not required to carry out the reduction process because the catalyst of Watanabe can be prepared prior to its use in the reduction reaction. See Watanabe at col. 20, lines 10-34. Applicants respectfully disagree.

As discussed above, Watanabe is silent with respect to the use of hydrogen gas as a hydrogen source. Additionally, an amide complex, as disclosed in Watanabe, which is obtained by treating a chloride complex with a base, can be isolated and can reduce ketones without the presence of a base by using a hydrogen donor, such as 2-propanol, as a hydrogen source. See Ohkuma I submitted with the November 12, 2009 Request for Reconsideration. Nevertheless, an ordinarily skilled artisan would not have reasonably expected that, using hydrogen gas as a hydrogen source, such a chloride complex can reduce ketones without the presence of a base. See Fujii submitted with the November 12, 2009 Request for Reconsideration.

In this regard, the Office Action, at pages 4-5, asserts that hydrogenation of a ketone compound with hydrogen gas is taught by Fujii at pages 2521 (left column, second paragraph) and 2522 (right column, lines 29-35). Applicants respectfully disagree. With respect to the description on page 2521, it describes a 98% ee and >99% yield of 1-phenylethanol (the reduced product) using 2-propanol, and not hydrogen gas, as a hydrogen source. With respect to the description on page 2522, it describes a 98% ee and >99% yield of 1-phenylethanol from the reaction of acetophenone with a 5:2 formic acid-triethylamine mixture under D<sub>2</sub> atmosphere. However, page 2522 further describes that only 0.08% and 0.18% of deuterium was incorporated at the C(1) and C(2) positions, respectively. An ordinarily skilled artisan would recognize from this fact that formic acid, as a hydrogen donor, served as the hydrogen

source for the asymmetric reduction and hydrogen gas played an insignificant role as a hydrogen source. Thus, an ordinarily skilled artisan would not have understood on Fujii to be evidence that hydrogen gas can be used to hydrogenate a ketone compound.

Furthermore, Ikariya discloses a ruthenium catalyst that is used for producing optically active alcohol compounds. See Abstract. The dichloride complex disclosed in Ikariya is not capable of functioning as a catalyst to hydrogenate ketones, using hydrogen gas as a hydrogen donor, without the presence of a base. In order for this dichloride complex to perform a catalyst reaction, the dichloride complex must be first reacted with a base to obtain a catalytically active species. However, such catalytically active species is unstable and cannot be isolated. Thus, an ordinarily skilled artisan would have recognized that such unstable compounds of Ikariya cannot be used to hydrogenate ketone compounds.

The August 21, 2009 Office Action, at page 4, asserts that Ikariya teaches that asymmetric hydrogenation of ketones could be accomplished using a ruthenium chloride catalyst with pressurized hydrogen or a hydrogen donor in the absence of a base. See Ikariya at paragraphs [0015] and [0040] - [0043]. Applicants respectfully disagree. Ikariya teaches that ruthenium complexes represented by the general formulae (1)-(4) can hydrogenate a carbonyl compound without the presence of a base under pressurized hydrogen if X and Y are hydrogen. See paragraph [0040]. Ikariya further teaches that, if X and Y are not hydrogen (e.g., a ruthenium chloride catalyst), a presence of a base is required for such ruthenium complexes to hydrogenate a carbonyl compound under pressurized hydrogen. Id. Thus, an ordinarily skilled artisan would recognize, in view of Ikariya, that asymmetric hydrogenation of ketones could not be accomplished using a ruthenium chloride catalyst in the absence of a base with any reasonable expectation of success.

In conclusion, Watanabe teaches hydrogenation of a ketone compound with a chloride complex and a base or with an amide complex, using a hydrogen donor, and not using

hydrogen gas. Ikariya teaches hydrogenation of a ketone compound with a catalyst obtained by a chloride complex and a base, using a hydrogen gas. Thus, the applied references do not disclose a process for producing an optically active alcohol by hydrogenating a ketone compound with a metal complex without the presence of a base under pressurized hydrogen.

For at least these reasons, the applied references, individually or in any combination, would not have rendered obvious claim 11. Claims 13, 17, 23, 26 and 29 depend from claim 11 and, thus, also would not have been rendered obvious by the applied references for at least the same reasons. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

**II. Conclusion**

In view of the foregoing, it is respectfully submitted that this application is in condition for allowance. Favorable reconsideration and prompt allowance of the claims are earnestly solicited.

Should the Examiner believe that anything further would be desirable in order to place this application in even better condition for allowance, the Examiner is invited to contact the undersigned at the telephone number set forth below.

Respectfully submitted,



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